DETERMINATION OF TEMPERATURE-PRESSURE PHASE DIAGRAMS:
CALIBRATION OF DTA SYSTEMS AND APLICATION TO ORGANIC MATERIALS

Scientific coordinator:
María del Barrio

Student:
Elena-Andreea Voicu
One of the major challenges of solid-state chemical physics in this century is to improve our ability to predict and control the appearance of different crystalline forms of a substance, the so-called "polymorphs". Polymorphism is the ability of a solid material to exist in more than one form or crystal structure. Polymorphism can potentially be found in any material including polymers, minerals and metals. Although polymorphs have different stability domains in temperature and pressure metastable polymorphs can make real appearance out of their stability domains appearing spontaneous transformations from the metastable (unstable form) to the stable form.

Polymorphism is important in the development of pharmaceuticals ingredients. Many drugs receive regulatory approval for only a single crystal form or polymorph. Polymorphism in drugs can also have direct medical implications. Medicine is often administered orally as a crystalline solid and dissolution rates depend on the exact crystal form or polymorph.

Generally the technique used for polymorph screening involve recrystallisation from a wide range of solvents under a variety of conditions: crystallisation in the presence of additives, co-crystallisation, hydrothermal methods. Another method that has proved to be successful for the exploration of polymorphism in molecular compounds is the use of high pressure techniques.

The aim of this project is to introduce the technique of differential thermal analysis (DTA), the information that this technique can provide and the procedures to be performed to obtain. This technique involves the measurements of relative changes in temperature when a substance is subjected to a controlled temperature heating/cooling rate. A calibration of the instrument’s response allows obtaining temperatures and heats related with the phase transitions. Basically the calibration procedure compares the known temperatures and heats of transitions of the reference materials with the measured values in every DTA device. For measures taken at normal pressure, details reports about the calibration procedures and the recommended reference materials have been published by the International Confederation of Thermal Analysis IUPAC.

When using a high pressure DTA, the evolution of the pressure during the phase transitions can be studied and the pressure-temperature (PT) phase diagram of a substance determined. In this work two high pressure DTA devices will be used to determine the PT phase diagrams of several organic compounds between 0.1 and 300MPa. The low temperature DTA can work between 200 and 373 K and the high temperature DTA functions between 300 and 450 K. Like in the conventional DTA, the sample is subjected to a controlled temperature program at several pressures, being the response of the device entirely similar. Although the calibration procedure used in conventional devices would be equally applicable in high-pressure instruments, the reviewed studies on the evolution of the temperatures and heats of transition with the pressure in reference materials are scarce. However, the Clasius-Clapeyron equation provides an alternative method for obtaining the transition’s heat of reference materials from measurements of high–pressure dilatometry. Both procedures will be tested for the calibration of two high pressure DTA.
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I.- Introduction

1.1 Thermodynamic concepts

To be able to understand the observed and measured phenomena, the fundamental thermodynamic concepts to describe the phase stability are introduced.

The state of a substance that can exchange with the exterior energy as heat or mechanical work is defined by three parameters: temperature (T), pressure (P) and specific volume (v). At any equilibrium state these parameters are constant. Depending on the values of two of these parameters, a substance can exist in one of the well know phases or states of the matter: solid, liquid or gas. For example, at normal pressure for temperatures below 0°C water is in a solid phase, for temperatures between 0°C-100°C in a liquid phase and above 100°C is gas. But at high pressures new solid phases are present in water, it want to say that water is a polymorph material.

Polymorphism, the existence of different solid phases, is common in the world of materials and together with conventional state changes, transitions between polymorphs may occur. They are evaluated in the same way that the conventional phase transitions, using the same thermodynamic concepts. In this paper we will focus upon the transitions between these polymorphic phases.

The thermodynamic function which allow us to determine the stability of a phase is the molar Gibbs free energy, defined as $G=H-TS$, where H and S are the molar enthalpy and entropy functions and T the temperature. From basics thermodynamics relationships the variation of this function ($dG$) can be expressed by the equation $dG = -SdT + VdP$. The magnitude of the S, V and G properties are well defined in an equilibrium state characterized by their pressure and temperature. Because G is function of P and T the representation of this function for every phase will be a surface in a tridimensional space (P, T and G) (see figure 1.1). The surface has a positive slope in the P direction and a negative slope in the T direction owing to the relations:\[1]\:

$$V = \left( \frac{\partial G}{\partial P} \right)_T \quad S = -\left( \frac{\partial G}{\partial T} \right)_P$$

The thermodynamics criteria for equilibrium requires that at fixed P and T the Gibbs free energy of a system must be at its lower value, then at every P and T the stable phase will be one whose Gibbs free energy is minimal. From the former criteria can be derived that equilibrium between two phases at determined P and T will be possible only if their molar Gibbs functions have equal value. In figure 1.1 two G surfaces are show, one for the α phase and other for the β phase. At the intersection of the two surfaces the phases α and β have equal values for their G function, then for these P T values both phases are in equilibrium. The projection of the intersection on the PT plane is the equilibrium curve between α and β phases. This curve divides the PT plane into two region: at one side α is stable with respect to β ($G^\alpha$ is lower than $G^\beta$) and at the other side β is stable with respect to α (see fig 1.1).
In figure 1.2 the projection of the $\alpha$ and $\beta$ Gibbs functions in isobaric (a) and isothermal (b) planes are shown. When one substance in phase $\alpha$ transform to the $\beta$ phase by means a change of temperature (a) or pressure (b) at the transition point no change in the $G$ function occurs. Nevertheless there are jumps in the derivatives of $G$ with respect to temperature and pressure that results in changes in the molar volume and molar entropy at the transition point (see relation [1]). This variation of entropy is related with the variation of the transition enthalpy or latent heat by means $\Delta H = T \Delta S$. Because of these discontinuities in the first derivatives of the $G$ function this kind of transitions are called first order transition (Ehrenfest classification). Vaporization, melting and the most of the polymorphs transitions can be included in this classification.
The equation, which relates the slope of P T transition curve and the discontinuities in entropy and specific volume at the point of transition, is known as the Clausius-Clapeyron equation:

\[
\frac{dP}{dT} = \frac{\Delta S}{\Delta V} = \frac{\Delta H}{T \Delta V}
\]

In terms of thermodynamics, there are two types of polymorphism. For a monotropic system, a plot of the free energy of the various polymorphs against temperature do not cross before all polymorphs melt; in other words, any transition from one polymorph to another will be irreversible. For an enantiotropic system, a plot of the free energy against temperature shows a crossing point before the various melting points, and it may be possible to convert reversibly between the two polymorphs on heating and cooling.

I.2 Thermal Analysis Techniques

Thermal analysis comprises a group of techniques in which a physical property of a substance is measured as a function of temperature, while the substance is subjected to a controlled temperature program. In the classical DTA and their subtle modification the heat–flux DSC the temperature difference developed between a sample and an inert reference material is measured when both are subjected to the same heat flux. However, the powder compensated DSC measures the difference in energy required to maintain the sample and reference at the same temperature when both are subjected to identical heating or cooling regimes. In spite to the different measuring principles they can be treated in a unified way.

The two types of DSC systems are shown in Figure 1.3. In power-compensation DSC the temperatures of the sample and reference are controlled independently using separate, identical furnaces. The temperatures of the sample and reference are made identical by varying the power input to the two furnaces; the energy required to do this is a measure of the enthalpy or heat capacity changes in the sample relative to the reference.

In heat-flux DSC, the sample and reference are connected by a low-resistance heat-flow path (a metal disc). The assembly is enclosed in a single furnace. Enthalpy or heat capacity changes in the sample cause a difference in its temperature relative to the reference; the resulting heat flow is small compared with that in differential thermal analysis (DTA) because the sample and reference are in good thermal contact. The temperature difference is recorded and related to enthalpy change in the sample using calibration experiments.
Figure 1.3.
Heat flux DSC and power compensation DSC

The signal obtained in these systems is called thermogram. This signal is a plotter of the differential temperature or power as a function of time or temperature (assuming that heating rate is knew). An endothermic event as the melting of the sample yields a peak on the DSC signal figure 1.4. The initial peak temperature $T_i$, is the temperature (at time $t_i$) where the curve begins to deviates from the initial base line; the final temperature $T_f$, is the temperature (at the time $t_f$) where the curve reaches the final baseline. The interpolated base line between these temperatures will be a horizontal straight line if the capacities of the solid and liquid phases are very similar. The temperature $T_0$ where the extrapolated ascending peak slope intersects the extrapolated initial base line is the extrapolated peak onset temperature.

In a DSC instrument the temperature sensors are not located in the sample, thus a temperature lag will be present between sensor and sample in both isothermal and temperature scanning mode. This thermal gradient will be enhanced under scanning conditions. Moreover another factors related with the sample, the mass, the layer thickness, the thermal conductivity, the heat transfer between sample and sample pan will affected the characteristic temperatures of the peak. Because of the difficulty to determine the initial peak temperature $T_i$ and the relatively small influence of the sample parameters in the extrapolated onset temperature $T_0$\(^5,6,7\), this temperature is read as the transition temperature and is used to defined the temperature scale of the DSC. The temperature scale is calibrated by comparing known temperatures of transition of reference materials with the measured temperature in the DSC system as a function of the heating rate.
Figure 1.4
Plot of heat flux against temperature to produce a microcalorimetric thermogram that corresponds to the melting of a pure substance.

The area of the peak defined by the interpolated baseline and the peak is proportional to the enthalpy of transition\(^5,6,7\). The enthalpy calibration\(^5,6,7\) allows to established the relationship between the enthalpy change measured (peak area \(\Delta H_{\text{meas}}\)) by the instrument for a given transition and the true transition enthalpy change of the sample \(\Delta H_{\text{tr}}\): \(\Delta H_{\text{tr}} = K \cdot \Delta H_{\text{meas}}\).

A detailed report about the calibration procedures and the recommended reference materials has been published for the International Confederation of Thermal Analysis IUPAC\(^8\).
REFERENCES:


II.- High-Pressure Differential Thermal Analysis (HP-DTA)

II.1.- Experimental system: Description

Like in the convectional DTA system in the high pressure DTA the sample and an inert reference are heated or cooled under identical conditions, at a determined pressure. Then, the analysis of the thermograms obtained at every pressure allows us to know the phase transitions presented by the sample in a determinate pressure-temperature range. This device aren’t commercially available and several systems has been developed in different laboratories (Ref). The system developed in the “Laboratori de caracterització de Materials” de la Universitat Politècnica de Catalunya is similar to those developed at the Bochum University1,3. Pression on the sample is exerted by a liquid that is introduced from a reservoir to a pump that can compress up to 300 MPa. This high pressure liquid is transferred to the calorimetric system which holds the sample through a capillary system. Manganin manometer allows to know the pressure at which the sample lies (figure 2.1).

![Scheme of the pressure transfer system](image)

Figure 2.1
Scheme of the pressure transfer system

To prevent the contamination of the sample by the pressure medium, the former, always in liquid phase, is confined in tin capsules (figure 2.2) which are closed avoiding air bubbles. The tin, easily deformable, transfer the medium pressure to the sample. The tin is founded in a suitable mould, afterwards a hole is bored so the capsule can be put onto the junctions of the thermocouple. One time the liquid
is filled into the capsule, this is squeezed in the upper part of this length. The sample and reference capsules are put in contact with K-type thermocouples connected in differential mode to determine the temperature difference between sample and reference. Another differential connection between the reference thermocouple and another in contact with ice allows us to measure the temperature. Both thermocouples are located within a capillary provided in one of its ends of the Bridgman piston (figure 2.3) that will be coupled to the calorimetric block or DTA cell (figure 2.4).

Figure 2.2.
The capsules and their thermocouple connection

Figure 2.3. Bridgman Piston
The Bridgman piston is the system that ensures the tightness of the fluid under high pressure in the calorimetric block. The essential part of the Bridgman piston is the ring in polytetrafluoroethylene (PTFE) or Teflon sandwiched between two metal parts. The Bridgman piston is composed by a fixed part (corundum) and a mobile part. When the high pressure liquid is introduced in the sample and reference zones, it moves up the Bridgman pistons, deforming the Teflon ring preventing oil leaks.

Two calorimetric blocks are available in the laboratory. The pressure transmission system is entirely similar in both but they are constructed of different materials that can work at temperatures below room temperature to 100K (low temperature DTA) or at temperatures above room temperature to 400K (high temperature DTA). The low temperature DTA is fitted into a tempering jacket made of copper. A liquid from a thermostat bath flows inside the jacket which regulates the temperature reached by the block and the sample.
The high temperature DTA is surrounded by a resistor that heats the block at a controlled rate. In both systems the block temperature is measured by means the reference thermocouple.

**II.2 Experimental system: Measurement Procedure**

Before doing our measurements the tin capsules must be manufactured. In a matrix, the tin is melted and once it has cooled the mold is removed. At the bottom of the capsule a hole of 2 mm deep approximately is made where the thermocouple will be housed. Once prepared the capsules, the sample must be introduced in liquid phase to avoid the presence of air into the capsule.

The sample and reference (empty) capsules are introduced into the DTA system and submitted to the selected pressure. The system is submitted to the controlled heating or cooling procedure. Heating rates of 2K/ min have been used.

By means an informatics programme the sampling time, the pressure, the temperature and the differential signal (temperature difference between sample and reference) are recorded.

In this experimental system the termogram is a representation of the differential signal versus reference temperature. (Figure 2.5).

![Differential Signal vs Temperature](image-url)

**Figure 2.5**
Differential signal versus temperature
The base line is adjusted by means a mathematical function, red curve in figure 2.6. From the graph the onset temperature, $T_0$, is determined and by means a calculation program the area between the peak and the base line is calculated. The units of the area are mV·s assuming that for every temperature we know the time by means the sampling time. This value will be transformed in energy units by the calibration procedure (next section).

![Figure 2.6](image.png)

**Figure 2.6**

Determination of the base line and onset temperature for the transition in the thermogram

When the heating ramp start one pressure is doing for the liquid over the sample but due to the expansion of the liquid when is heated the pressure increases with temperature. The real pressure of the sample when the transition occurs, at $T_0$, must be calculated from the evolution of the pressure with the temperature (see figure 2.7). By means this procedure the evolution of the transition temperatures with the pressure is determined, which is the information represented in the diagram temperature-pressure (PT).
II.3 Experimental system: Calibration

By means the calibration procedure the energy associated with a thermal effect can be know. The data used for calibration of both devices have been obtained from different techniques, dilatation measurements in pressure or PVT measurements for the low temperature DTA and Differential Scanning Calorimetry in pressure for the high temperature DTA.

The pressure transmission medium have been oils from Hubber and Lauda trading houses. The oil from Lauda, Kryo 85, can work between -80 and 35 °C. The oil from Hubber, Hubber 90, presents a wider working temperatures range from -90 to 200 °C. In the low temperature DTA measurements with both oils have been performed. The influence physical properties like the heat capacity and the thermal conductivity in the heat transmission could affect the calibration constants values. The liquid Hubber has been employed in the high-temperature DTA which allow to evaluate the evolution of the calibration constant in a wider range of temperatures assuming that we have the same detectors in both DTA systems.

Figure 2.7
Evolution of the pressure versus temperature.
II.3.1 Low temperature DTA calibration.

The calibration compound has been Tert butyl Nitro (TBN). At normal pressure this compound shows polymorphism, the low temperature phase (III) transforms to a second phase II at 216.4K that transform upon heating in a new phase I at 260K that melt at 298.5 K\(^4,6\). All the transitions are reversible, then an enantiotropic relation exist between the three phases. Dilatation measurements (PVT)\(^4\) performed until 300Mpa allows to determine the stability domains of these phases and PT diagram (figure 2.8) and the volume variation at every pressure for III-II and II-I transitions. The application of the Clausius-Clapeyron enable to know the evolution of the transitions enthalpies for both transitions in the former pressure range (figure 2.9).

![PT diagram of TBN obtained from PVT measurements](image)

Fig 2.8

PT diagram of TBN obtained from PVT measurements
The measurements have been performed over four independents samples. The evolution of the transitions temperatures with the pressure agree with bibliographic values (Fig 2.10) for both pressure oils. Any influence of the compressor oil in the temperature values has been observed.

To evaluate the calibration constant only the III-II transition has been employed. For every pressure the experimental enthalpy value (H (mv·s/mol)) has been calculated and compared with the theoretical value (from PVT measurements), H bibli( J/mol), at the same pressure (Table 2.1). The quotient between them is the calibration constant K (Figure 2.11).
Evolution of the III-II and II-I transitions temperatures with the pressure for the samples A,B (Kryo) and C,D (Hubber). The curves are ajusts of the bibliographic values.

<table>
<thead>
<tr>
<th>P/Mpa</th>
<th>K(J/mv*s)</th>
<th>h(mv*s/mol)</th>
<th>H bib(j/mol)</th>
</tr>
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<tr>
<td>0.66</td>
<td>1.07</td>
<td>3956.50</td>
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<td>1.05</td>
<td>4122.78</td>
<td>4334.78</td>
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<td>105.09</td>
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<td>252.02</td>
<td>1.45</td>
<td>3724.81</td>
<td>5395.19</td>
</tr>
</tbody>
</table>

Evolution of enthalpies values (experimental and bibliographic) for the III-II transition and the evolution of the calibration constant K with the pressure being Kryo 85 the transmission medium.
Evolution of the calibration constant K with pressure for the transmission medium Kryo 85

This K value has been applied to the enthalpy values measured for the II-I transition (mv.s / mol) and compared with the bibliographic values (Figure 2.11). By means this procedure the influence of the contact capsule-termocouple is minimized. The maximum discrepancy between measured and theoretical values is less than 20%. This minimal (1% -5%) discrepancy is obtained for high values of pressure which is consistent with the fact that high pressure improves contact.
The same procedure has been applied to the compressor oil Hubber. In the figure 2.13 are shown, for an easier comparison the K values obtained with both oils. The liquid Hubber presents K values higher than Kryo oil for the entire pressure range studied, and its evolution with pressure is also higher. Although manufacturers of any of them included in the specification composition and thermal properties the results obtained suggest that the oil Hubber has higher thermal conductivity.

Figure 2.12
Evolution of enthalpies values (experimental after conversion by means the calibration constant K and bibliographic) for the II-I transition with pressure being Kryo 85 the transmission medium.

\[ y = -0.02x^2 + 1.748x + 4649, \quad R^2 = 1 \]
**Fig 2.13**
Evolution of the calibration constant $K$ with the pressure for both transmission mediums Kryo 85 and Hubber.

**Figure 2.14**
Evolution of enthalpies values (experimental after conversion by means the calibration constant $K$ and bibliographic) for the II-I transition with pressure being Hubber the transmission medium.
The discrepancies found between theoretical and calculated values for the transition II-I are too high (30%) (Figure 2.14). Therefore the study of this oil cannot be considered finished and in the future new measures will be made.

II.3.2 High temperature DTA calibration.

The compound chosen for calibration of high-temperature DTA has been the n-alkane C20 (C\textsubscript{20} H\textsubscript{42}). At normal pressure has a single solid phase\textsuperscript{7}, (Triclinic structure) that melts at the temperature of 309.7 K with an enthalpy variation of 68.1 kJ·mol\textsuperscript{-1}. Studies in pressure to 300 Mpa\textsuperscript{3,5} in the family of the n-alkanes with even number of carbon atoms does not reveal the existence of other polymorphic form in the above pressure range.

The liquid employed as pressure transmitting medium has been the liquid Hubber and the heating runs have been performed at 2K/min. The evolution of melting temperatures with the pressure of the compound C20 limits the calibration results to the lower range of temperatures of the device. Despite this limitation, we could compare the values of the calibration constant obtained in both DTA with the same compressor fluid for methodologies and transitions markedly different.

The measurements have been realized over two independent samples, series 1 and 2 in figure 2.15. The obtained slope value (0.176 K·Mpa\textsuperscript{-1}) is of the same order of magnitude as those obtained in other even n-alkanes\textsuperscript{5}. In the table 2.2 the measured enthalpies values (mv·s/mol) and calculated from bibliographic results\textsuperscript{5} (J/mol) for every measured pressure are show with the corresponding K values.

<table>
<thead>
<tr>
<th>P/Mpa</th>
<th>h(mv*s/mol)</th>
<th>hbibli(J/mol)</th>
<th>K(J/mv*s)</th>
</tr>
</thead>
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<td>13.08</td>
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<td>1,27</td>
</tr>
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<td>100,82</td>
<td>44395,96</td>
<td>74384,95</td>
<td>1,68</td>
</tr>
</tbody>
</table>

Table 2.2

Melting enthalpies values (experimental and bibliographic) at several pressures for for the n-alkane C\textsubscript{20}H\textsubscript{42} together with their corresponding calibration constant values K.
Figure 2.15

PT phase diagram for the n-alkane C_{20}H_{42}

The evolution of the calibration constant as a function of the pressure has been represented in figure 2.16 for both DTA systems. Assuming that the K values are in error at least of the same order of magnitude as measured enthalpy (around 10% of its value) we can be established similar evolution for the K value regardless of the temperature range.
II.3.3 Conclusions

Obtaining temperatures and enthalpies of transition through thermal systems such as a DTA requires a previous calibration. For systems operating at normal pressure protocols and calibration substances are well established. Not so for systems of the same nature working at high pressures possibly because they are not commercial systems and few laboratories have them.

This paper has attempted to probe two different methodologies for the calibration of DTA, from measurements of expansion or PVT data and from DSC measurements at high pressure. Although DTA and DSC are colorimetric systems that can provide the same type of information the measurement accuracy is higher enthalpy in the DSC.

In the low temperature ATD, tests were carried out with two compressors media types. With respect to temperature measurements any influence of the fluid compressor is observed in the values obtained and the results match those from the literature. We conclude that the thermoelectric power of thermocouples, provided by the manufacturer at normal pressure does not change with pressure. With respect to the enthalpy values measured and consequently the energy calibration factors calculated, the values obtained with the liquid Kryo show greater repeatability. The high dispersion of
values obtained for the liquid Hubber in both DTA requires us to interpret with caution the results obtained.

One problem that can occur in these devices is the compressor fluid filtration through the walls of the capsule, which could be a cause to justify the dispersion of measured values. In addition the behaviour of these liquids under pressure is unknown.

New oil compressors will be tested in order to establish the best conditions of measurement in both systems.

REFERENCES


